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Sensitivity and Specificity of Concealed Entrainment for the Identification of a Critical Isthmus in the Atrium: Relationship to Rate, Anatomic Location and Antidromic Penetration

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OBJECTIVES This study was designed to determine the sensitivity and specificity of concealed entrainment (CE) for the identification of a critical isthmus in the atrium.

BACKGROUND Isthmus identification during entrainment mapping of macro-reentrant atrial tachycardia (MRAT) relies on the demonstration of CE.

METHODS Using the model of typical atrial flutter, entrainment was performed in 10 patients at four rates (flutter cycle length [FCL] minus 10/20/30/40 ms) from seven sites: isthmus entrance/exit, low lateral/high lateral/high septal right atrium and proximal/distal coronary sinus. Surface 12-lead electrocardiogram fusion was evaluated by three observers blind to patient status. The extent of antidromic penetration (AP) was measured off the pacing catheter positioned around the tricuspid annulus.

RESULTS The sensitivity for CE identifying any isthmus site was greatest at FCL−10 (100%), but the specificity was poor (54%). Conversely, specificity was greatest at FCL−40 (98%), but the sensitivity was poor (65%), with manifest entrainment (ME) observed from the isthmus entrance in 70% of episodes. At FCL−30, sensitivity (85%) and specificity (90%) were "balanced," but CE still resulted during entrainment from a non-isthmus site in five of 10 patients. Antidromic penetration increased with pacing CL shortening ($p < 0.001$) and correlated with the development of ME ($p < 0.001$). Antidromic penetration was significantly blunted from the isthmus exit compared to all other sites ($p = 0.003$).

CONCLUSIONS The sensitivity and specificity of CE for identifying an isthmus in the atrium are critically dependent on the pacing rate and the precise anatomic pacing site within the isthmus. These findings may have implications for the use of entrainment in the mapping of unknown MRAT circuits. (J Am Coll Cardiol 2002;39:896–906) © 2002 by the American College of Cardiology Foundation

Since the original descriptions by Waldo and others on the nature of entrainment and criteria for determining its presence (1–4), continuing work by the same group and others has created a paradigm for the use of entrainment mapping in evaluating macro-reentrant circuits in the atrium and ventricle (5–8). In particular, as described by Stevenson et al. (6), the observation of concealed entrainment (CE) has developed as an important criterion for identifying a narrow isthmus within the tachycardia circuit that is critical for tachycardia maintenance and an optimal target for radiofrequency ablation (RFA) (9–12).

Although entrainment mapping has proved to be an important adjunctive tool during ablation of ventricular arrhythmias, the predictive value of CE in isolation for identifying a successful ablation site has been relatively low (6,13). In the landmark study by Stevenson et al. (6), the positive predictive value of the observation of CE associated with a post-pacing interval (PPI)-tachycardia cycle length (TCL) <30 ms for successful ablation of ventricular tachycardia in the presence of scar was only 25%. During atrial macro-reentry there is a relative paucity of data describing the utility of CE for identification of a narrow isthmus.

The aim of the present study was to prospectively characterize the specificity and sensitivity of CE for identifying an isthmus in the atrium. We also explored the effect of entrainment rate, anatomic relationship of the pacing site to the isthmus and extent of antidromic penetration (AP) of the circuit on the demonstration of fusion on the surface electrocardiogram (ECG). We used typical counter-clockwise atrial flutter (AFL) as the model for this study because the critical components of this circuit have been extensively described (10,14–17).

METHODS

Study population. Patients undergoing curative RFA of typical counter-clockwise isthmus-dependent chronic AFL with visible exposed flutter (F) waves were enrolled in the study. To ensure visualization of the F-waves, antiarrhythmic atrioventricular (AV) nodal blocking agents were not discontinued, but all other antiarrhythmic agents were

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Abbreviations and Acronyms

AFL = atrial flutter
AP = antidromic penetration
AV = atrioventricular
CE = concealed entrainment
CS = coronary sinus
DCS = distal coronary sinus
ECG = electrocardiogram
FCL = flutter cycle length
HLRA = high lateral right atrium
HSRA = high septal right atrium
LAO = left anterior oblique
LLRA = low lateral right atrium
ME = manifest entrainment
PCS = proximal coronary sinus
PPI = post-pacing interval
RA = right atrium
RFA = radiofrequency ablation
TA = tricuspid annulus
TCL = tachycardia cycle length

ceased five drug half-lives before the procedure. All patients gave written informed consent and the research protocol was approved by the ethics committee of the Royal Melbourne Hospital Research Foundation.

Definitions. MANIFEST ENTRAINMENT (ME). The acceleration of AFL to the particular pacing rate (capture of the reentrant circuit) with evidence of constant fusion in the F-wave morphology as assessed by a standard 12-lead ECG. Upon termination of pacing there is spontaneous resumption of AFL (i.e., the tachycardia has not been terminated), and the last paced beat is always entrained but not fused. The findings of constant fusion and progressive fusion (different degrees of constant fusion at different pacing rates) confirm the presence of a reentrant circuit with an excitable gap. These findings represent fulfillment of the first and second criteria for establishing the presence of transient entrainment (18).

CONCEALED ENTRAINMENT. Concealed entrainment is the acceleration of AFL to the particular pacing rate (capture of the reentrant circuit) without evidence of fusion in the F-wave morphology as assessed by a standard 12-lead ECG. The diagnosis of CE can only be made after ME has been demonstrated at another site to prove the existence of a reentrant circuit with an excitable gap.

ISTHMUS ENTRANCE. The isthmus entrance is a site within the cavo-tricuspid isthmus in its lateral region at approximately 6:30 when viewed in the left anterior oblique (LAO) projection.

ISTHMUS EXIT. The isthmus exit is a site in the cavo-tricuspid isthmus in its medial region at approximately 5:00 when viewed in the LAO projection. The coronary sinus (CS) ostium was designated 4:00 in this projection.

Electrophysiologic study. CATHETER POSITIONING. Venous access was obtained via the right femoral vein and right internal jugular vein (for the CS catheter). A 20-pole tricuspid annulus (TA) catheter was positioned in the right atrium (RA) parallel to the TA such that the distal pole was located in the medial region of the cavo-tricuspid isthmus (inter-electrode spacing 2 mm and inter-bipole spacing 5 mm: "2–5–2"). A decapolar catheter was positioned in the CS (electrode spacing 2–5–2 mm) with the proximal bipole positioned 1 cm distal to the CS ostium as determined in the LAO projection. A quadripolar catheter was positioned to record a His bundle electrogram. Intracardiac signals and a standard 12-lead ECG were displayed on a computerized mapping system and recorded to optical disk.

ENTRAINMENT PROTOCOL. The study protocol was performed before RFA. Pacing was performed from seven anatomic sites (two within the isthmus and five outside the isthmus) defined by fluoroscopic visualization of the RA using standard left and right anterior oblique projections.

- Isthmus exit: TA bipole 1/2.
- Isthmus entrance: TA bipole 5/6.
- Low lateral right atrium (LLRA): TA bipole 9/10.
- High lateral right atrium (HLRA): TA bipole 13/14 or 15/16.
- High septal right atrium (HSRA). (Before pacing from the HSRA the 20-pole catheter was repositioned so that the distal bipole was adjacent to the mid-lateral RA. Pacing was then performed from TA 13/14 or 15/16, which was now at the HSRA region. This allowed an assessment to be made of the degree of AP resulting from the HSRA paced antidromic wave front.)
- Proximal CS (PCS): CS bipole 9/10.
- Distal CS (DCS): CS bipole 1/2.

The cycle length (CL) of the AFL was measured (flutter cycle length, FCL) and entrainment performed at 10, 20, 30, and 40 ms below the FCL (FCL−10, FCL−20, FCL−30 and FCL−40). For each site and CL, pacing was performed three times. Pacing was performed at twice the local capture threshold determined during pacing at a rate faster than the FCL. If the local capture threshold was >2.5 mA, the position of the TA catheter was moved to ensure better atrial wall contact. Each episode of pacing was performed until steady-state entrainment was achieved for 5–8 s as determined by the presence of a consistent relationship between the pacing stimulus artifact and the atrial electrograms and a constant unchanging paced F-wave morphology.

For each episode the post-pacing interval (PPI) was measured as the interval from stimulus artifact to onset of the initial sharp deflection of the first post-pacing electrogram. An offline analysis of the PPI minus the FCL was made after each episode of entrainment. If the F-waves during pacing were obscured by the QRS complex or T-wave, an AV blocking agent (digoxin 250 to 500 μg or atenolol 2.0 to 5.0 mg) was administered intravenously.

At completion of the research protocol all patients underwent conventional isthmus ablation with confirmation of bidirectional isthmus block.

DETERMINATION OF CONCEALED ENTRAINMENT. For each episode of entrainment a high quality copy of the ECG was printed showing the F-wave morphology both during and after pacing. The ECG was displayed at 50 mm/s speed with the signals gained to a level of 25 mm/mV to allow a clear appreciation of the F-wave morphology. Electrocardiogram traces were then reviewed by three electrophysiologists blind to the site and rate of pacing. The paced F-waves in each of the 12 surface ECG leads were evaluated for amplitude, duration and morphology and compared to the non-paced F-wave. The episode of entrainment was defined as concealed when there was an exact match in all 12 surface ECG leads. For episodes where there was a disagreement among the three reviewers, the majority opinion was deemed correct. The inter-observer variability for the description of CE was calculated.

ANTIDROMIC PENETRATION. The number of bipoles antidromically penetrated by the paced activation wave front was measured from the 20-pole TA catheter for each of the sites excluding the proximal and DCS. A bipolar recording site was considered to have been penetrated by the antidromic wave front when the following criteria were constantly present during entrainment: 1) electrogram advancement by ≥10 ms compared with timing during AFL; 2) change in activation sequence (reversal of the activation sequence from the entrained site); and 3) change in electrogram morphology (4).

The distance of antidromic capture (mm) was measured from the center of the stimulating bipole pair to the center of the furthermost antidromically penetrated bipole. All measurements of electrogram timing were made offline using on-screen calipers at 400 mm/s sweep speed. The onset of the bipolar electrogram was taken as the onset of the initial sharp deflection.

STATISTICS. Continuous data are expressed as mean ± 1 SD. Proportions are expressed as percentages with 95% confidence intervals (CI) (19). To determine the sensitivity and specificity a conventional 2 × 2 matrix (A/B/C/D) was constructed for each rate of entrainment where A = true positive result (CE when pacing an isthmus site); B = false positive result (CE when pacing a non-isthmus site); C = false negative result (ME when pacing an isthmus site); and D = true negative result (ME when pacing a non-isthmus site). Hence sensitivity = A/(A + C) and specificity = D/(B + D). The effect of entrainment CL on sensitivity and specificity was determined using logistic regression analysis for ME versus CE predicted by patient, site and rate. The effect of pacing site and rate on the degree of AP was determined by performing a two-factor (rate and site) analysis of variance. The relationship between the extent of AP and surface ECG fusion (expressed at two levels: CE or ME) was determined by extending the analysis of variance to include fusion as a third factor. Multiple comparisons were performed using Tukey pairwise comparisons. Inter-observer variability for the description of CE versus ME was determined by calculating κ (the kappa coefficient) (20). A p value of <0.05 was considered significant. Statistical analysis was performed using commercially available software: Minitab (Minitab Inc., State College, Pennsylvania) and LogXact (Cytel Software Corp., Cambridge, Massachusetts).

RESULTS

Patient characteristics. Ten males of mean age 69 ± 7 years with chronic AFL formed the study population. Other than mild to moderate biatrial enlargement, seven patients had structural heart disease (five with prior myocardial infarction, one with left ventricular hypertrophy and one with dilated cardiomyopathy). Two patients had a permanent pacemaker (one with previous AV node ablation). The mean FCL was 248 ± 34 ms.

PPI-FCL. During entrainment from sites within the flutter circuit, the mean PPI-FCL was ≤30 ms for all four pacing rates. The PCS pacing site was within the AFL circuit in five of 10 patients and outside the AFL circuit in the remainder (mean PPI-TCL ≥58 ms). The DCS pacing site was outside the AFL circuit in eight of eight patients (mean PPI-TCL ≥97 ms). There was no evidence of significant lengthening of the PPI during entrainment at faster (FCL−40) as compared with slower (FCL−10) rates when pacing from the HSRA (FCL−10 vs. FCL−40: 22 ± 13 vs. 26 ± 20 ms, p = ns), HLRA (25 ± 11 vs. 27 ± 18 ms, p = ns), LLRA (25 ± 18 vs. 29 ± 17 ms), isthmus entrance (21 ± 11 vs. 25 ± 19 ms, p = ns) or in those patients where the PCS was in the circuit (23 ± 16 vs. 26 ± 18 ms, p = ns). However, during entrainment from the isthmus exit a small but statistically significant lengthening in the mean PPI was observed (FCL−10 vs. FCL−40: 14 ± 14 vs. 21 ± 19 ms, p = 0.02). Despite this lengthening, the site was still within the circuit based on a definition of PPI-TCL <30 ms. In addition, lengthening of the mean PPI was observed during entrainment from the PCS in those five patients where this site was outside the flutter circuit (59 ± 13 vs. 73 ± 13 ms, p = 0.04).

Concealed entrainment. The standard 12-lead surface ECG recordings of 272 episodes of entrainment were classified as concealed (C) (n = 107) or manifest (M) (n = 165). In two patients entrainment was not performed from the DCS. The percentage of entrainment episodes classified as CE is presented in Figure 1 according to the site and rate of entrainment pacing.

There was a highly significant effect of pacing rate on both sensitivity and specificity as the CL of the entrainment rate shortened (p = 0.001 for sensitivity, p < 0.001 for specificity; Table 1). At FCL−10 the sensitivity was greatest (100%), but associated with a low specificity (54%; CI 40% to 58%). At FCL−10, false positive CE resulted from pacing 22 non-isthmus sites in 10 patients (Fig. 2). Concealed entrainment did not result from pacing any sites outside the AFL circuit. As the pacing CL shortened, the

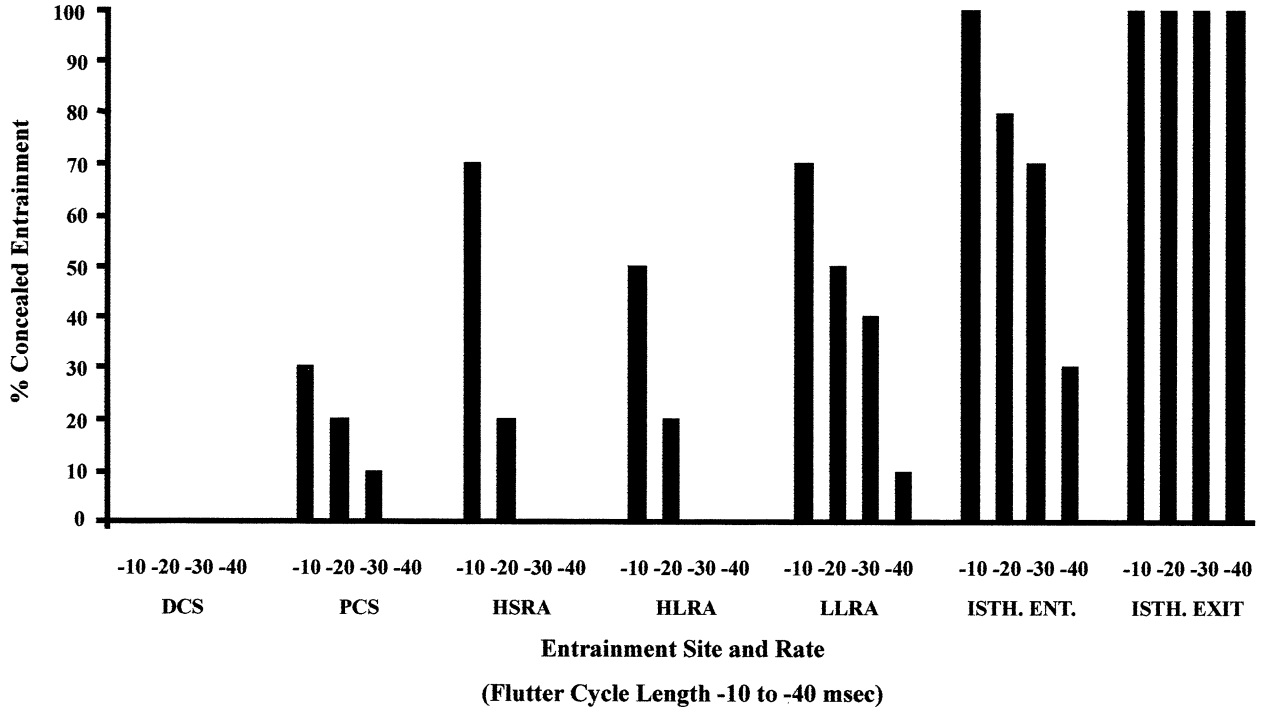

Figure 1. Percentage of entrainment episodes diagnosed as concealed entrainment according to the site and rate of pacing. DCS = distal coronary sinus; PCS = proximal CS; HSRA/HLRA/LLRA = high septal/high lateral and low lateral right atrium; ISTH ENT = isthmus entrance; ISTH EXIT = isthmus exit.

number of false-positive results for CE decreased (one false positive at FCL−40 with CE resulting from pacing the LLRA), and there was a progressive increase in the specificity. At FCL−40 the specificity was 98% (CI 94% to 102%); However, at this CL there was an associated decline in the sensitivity (65%; CI 44% to 86%) because of ME resulting from entrainment from the isthmus entrance in seven of 10 patients (Fig. 3). Manifest entrainment was not recorded from the isthmus exit at any CL in any patient (Fig. 4).

Antidromic penetration. Antidromic penetration results are presented graphically in Figure 5. There was a highly significant effect of entrainment rate ($p < 0.001$) on the degree of AP. With progressive shortening of the entrainment CL, a significant increase in the degree of AP was observed ($p < 0.002$ for all comparisons: FCL−10 vs. FCL−20, FCL−20 vs. FCL−30 and FCL−30 vs. FCL−40).

The site of entrainment was also significantly associated with the degree of AP ($p < 0.001$), though this effect was largely accounted for by the reduced extent of AP recorded during entrainment from the isthmus exit as compared to all other sites. There was no significant difference between the AP observed at the HSRA, HLRA and LLRA. When pacing from the isthmus entrance, there was a significant difference between this site and the HLRA ($p = 0.002$), but not the HSRA or LLRA. The degree of AP produced during isthmus exit pacing was significantly less when compared to all other sites ($p = 0.003$ for isthmus exit vs. HSRA, HLRA, LLRA and isthmus entrance). In addition, when pacing from the isthmus exit at FCL−40, the mean AP (9 ± 3 mm) was 47% less than that resulting from pacing the isthmus entrance (17 ± 5 mm) at the same rate. Some degree of AP resulting from pacing the isthmus exit was recorded in nine of 10 patients. In one of 10 patients there was no AP at any rate of entrainment from the isthmus exit (Fig. 4); However, in the same patient 18 mm of AP was recorded during pacing from the isthmus entrance at FCL−40.

There was a highly statistically significant relationship between the degree of AP and the documentation of entrainment as either concealed or manifest ($p < 0.001$). Adjusting for site and rate, episodes resulting in ME were

Table 1. Effect of Rate on the Sensitivity and Specificity of Concealed Entrainment for the Identification of an Isthmus Site

	All CL	FCL–10	FCL–20	FCL–30	FCL–40	p Value
% Sensitivity	85 (77–93)	100	90 (77–103)	85 (69–101)	65 (44–86)	0.001
% Specificity	80 (74–86)	54 (40–58)	77 (65–89)	90 (82–98)	98 (94–102)	< 0.001

Values presented with 95% confidence intervals.
CL = cycle length; FCL = flutter cycle length.

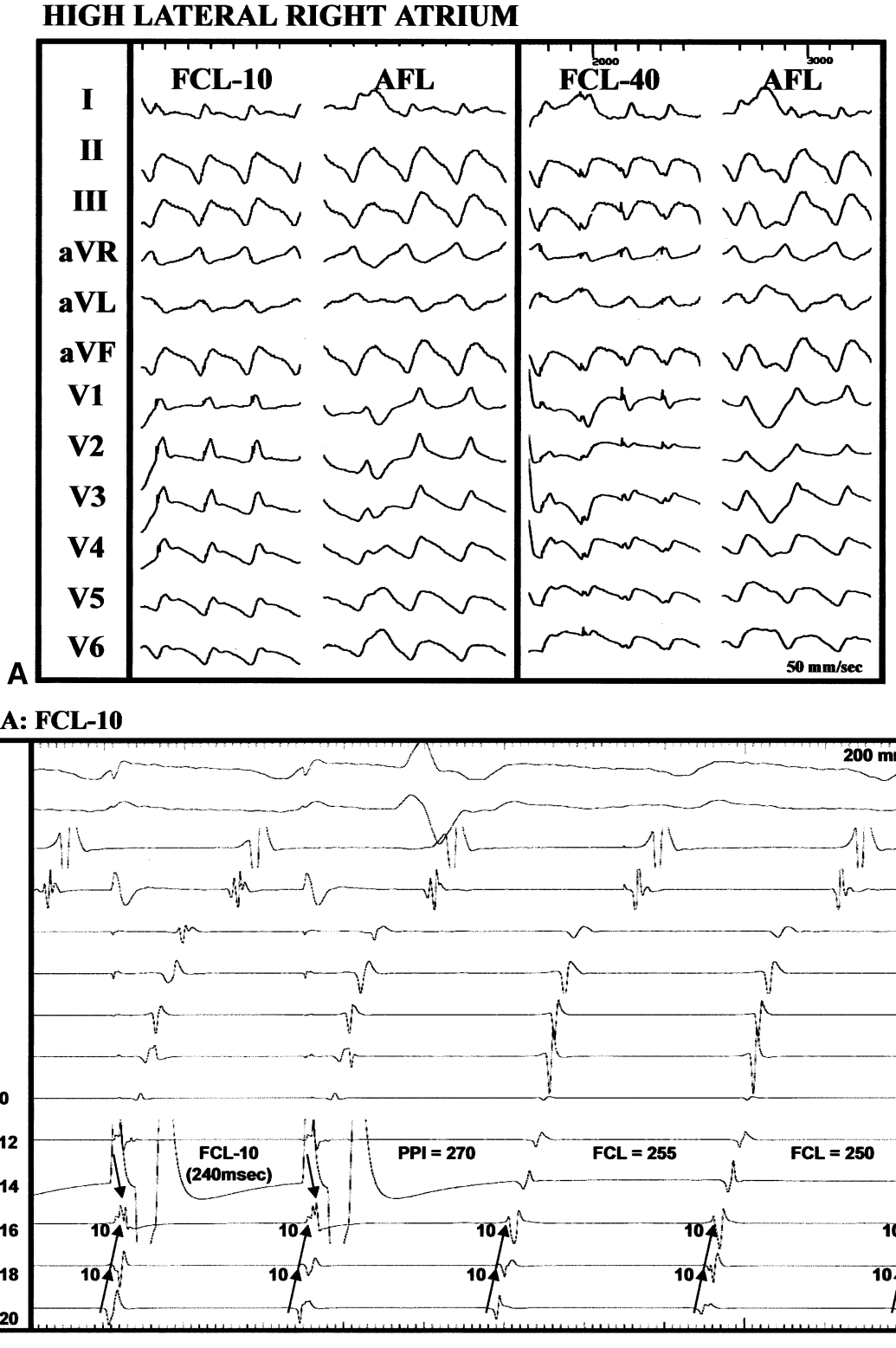

Figure 2. Entrainment from the high lateral right atrium (HLRA). **(A)** Electrocardiogram (ECG) recorded during entrainment from the HLRA at flutter cycle length (FCL)-10 and FCL−40 compared to the non-paced flutter wave. At FCL−10 the paced flutter wave appears identical to the non-paced flutter wave in the limb leads, with minor differences in amplitude and morphology observed in the anterior leads (V1 to V6). Three blinded observers recorded this as concealed entrainment. At FCL−40 the paced flutter wave is clearly different and was recorded as manifest entrainment by all three observers. **(B)** Intracardiac electrogram recording during entrainment at FCL−10 ms from the HLRA (TA 13/14). The post-pacing interval (PPI) minus FCL is 15 ms, confirming that the HLRA is within the circuit. The upward arrows indicate the orthodromic activation times from TA 19/20 to 17/18 (10 ms) and TA 17/18 to 15/16 (10 ms) are unchanged during entrainment consistent with orthodromic capture of TA 17/18 and 15/16. However, the entrained TA 15/16 electrogram is different in morphology from the non-entrained electrogram, suggesting fusion between the antidromic **(downward arrows)** and orthodromic**(upward arrows)** wave fronts at this point. Also shown: surface ECG leads II and III, and distal and proximal coronary sinus (DCS/PCS) recordings.

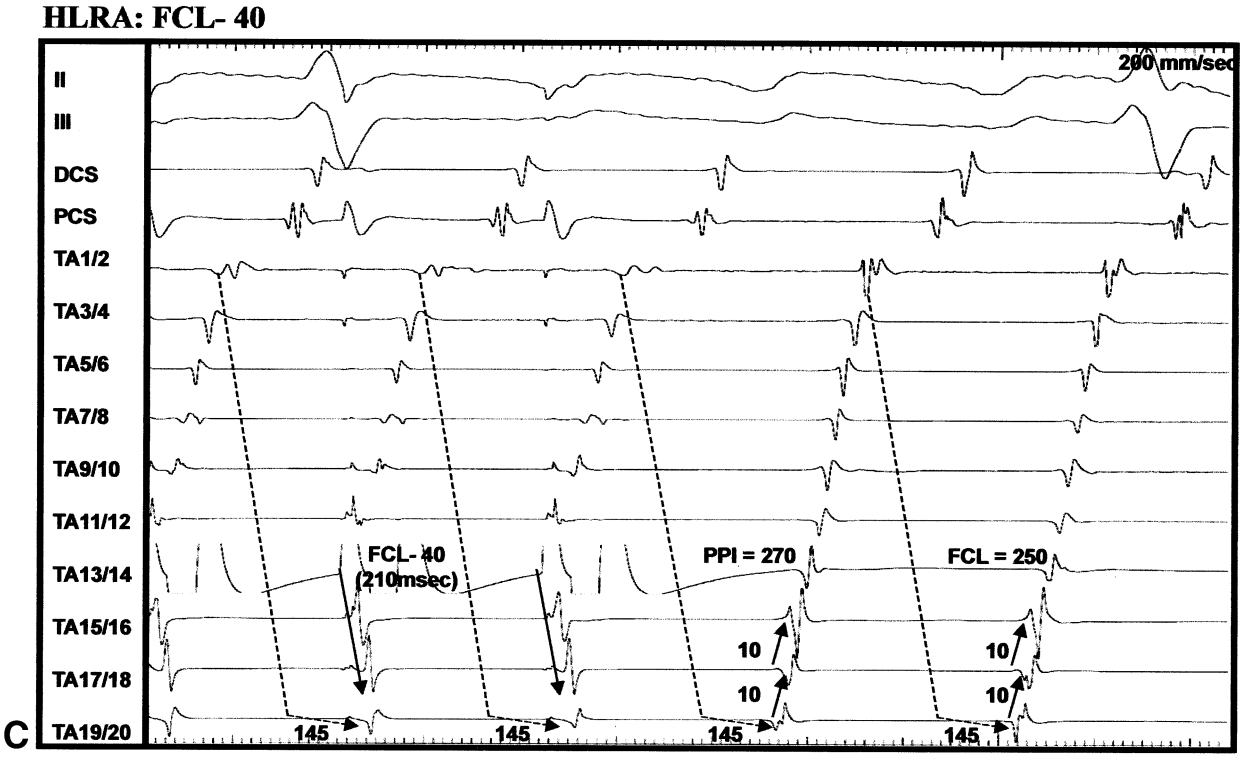

Figure 2. (*continued*) **(C)** Entrainment at FCL−40 ms from the HLRA. The PPI minus FCL is 20 ms, confirming that the HLRA is within the circuit. TA 15/16 and 17/18 are now captured by the antidromic wave front **(solid downward arrow),** with associated electrogram morphology change and activation timing ahead of TA 19/20, which is still orthodromically activated with activation timing and morphology not significantly different from spontaneous flutter **(dashed downward line from TA 1/2 to TA 19/20)**. The phenomenon described by Cosio et al. (17) of orthodromic overlap is also evident with orthodromic activation of TA11/12 and 9/10 (by the *n* wave front) occurring simultaneously with orthodromic activation (by the previous *n−1* wave front) of TA 19/20. Surface ECG fusion may be a "fusion" of these two processes (antidromic penetration and orthodromic overlap), though in the present analysis the observation of manifest entrainment was statistically related to the extent of antidromic penetration.

associated with a greater degree of AP (95% CI: 2–6 mm) than those episodes resulting in CE.

Inter-observer error. There was a high degree of correlation among each of the three observers for the description of the ECG during entrainment as either ME or CE: $\kappa = 0.8$ for observer 1 and 2, $\kappa = 0.9$ for observer 1 and 3 and $\kappa = 0.9$ for observer 2 and 3.

DISCUSSION

Main findings. In patients with typical counter-clockwise isthmus-dependent AFL, this prospective study has systematically analyzed the relationship between entrainment rate, anatomic location, extent of AP and presence of surface concealment. The following key findings have been demonstrated:

1. Entrainment from sites in the circuit will frequently produce concealed fusion at a longer entraining CL even when not in a critical isthmus.
2. Entrainment from the isthmus entrance may produce manifest fusion at a shorter entraining CL because of AP out of the isthmus.
3. Entrainment from the isthmus exit always produces concealed fusion, not only because AP is confined within the isthmus, but also because the extent of AP is less than that observed at other sites for a similar entraining CL.
4. Entrainment from sites outside the circuit produces manifest fusion at all entraining CLs.
5. At entraining rates up to 40 ms less than the FCL used in this study, decrement within the circuit was minor and did not lead to sites "in" the circuit appearing to be "out" based on the PPI-TCL.

A highly statistically significant relationship was shown to exist between the degree of AP and each of the following factors: pacing rate, pacing site and presence or absence of CE on the surface ECG.

Utility of entrainment mapping: comparison with other studies. Many clinical studies have determined the sensitivity of CE for identifying an isthmus and RFA target site during entrainment mapping of macro-reentrant ventricular tachycardias (6,12,13). The predictive value of CE in isolation for identifying an isthmus has generally been low and has required the addition of other parameters to increase it.

Fewer studies have evaluated CE in the atrium (7,21). Bogun et al. (21) performed entrainment mapping and RFA of atypical AFL in a population without prior cardiac surgery. When pacing was at 10 to 30 ms below the FCL, the predictive value of CE for identifying a successful RFA site was only 45%. This increased to 75% in the presence of matching electrogram-F and stimulus-F intervals or if

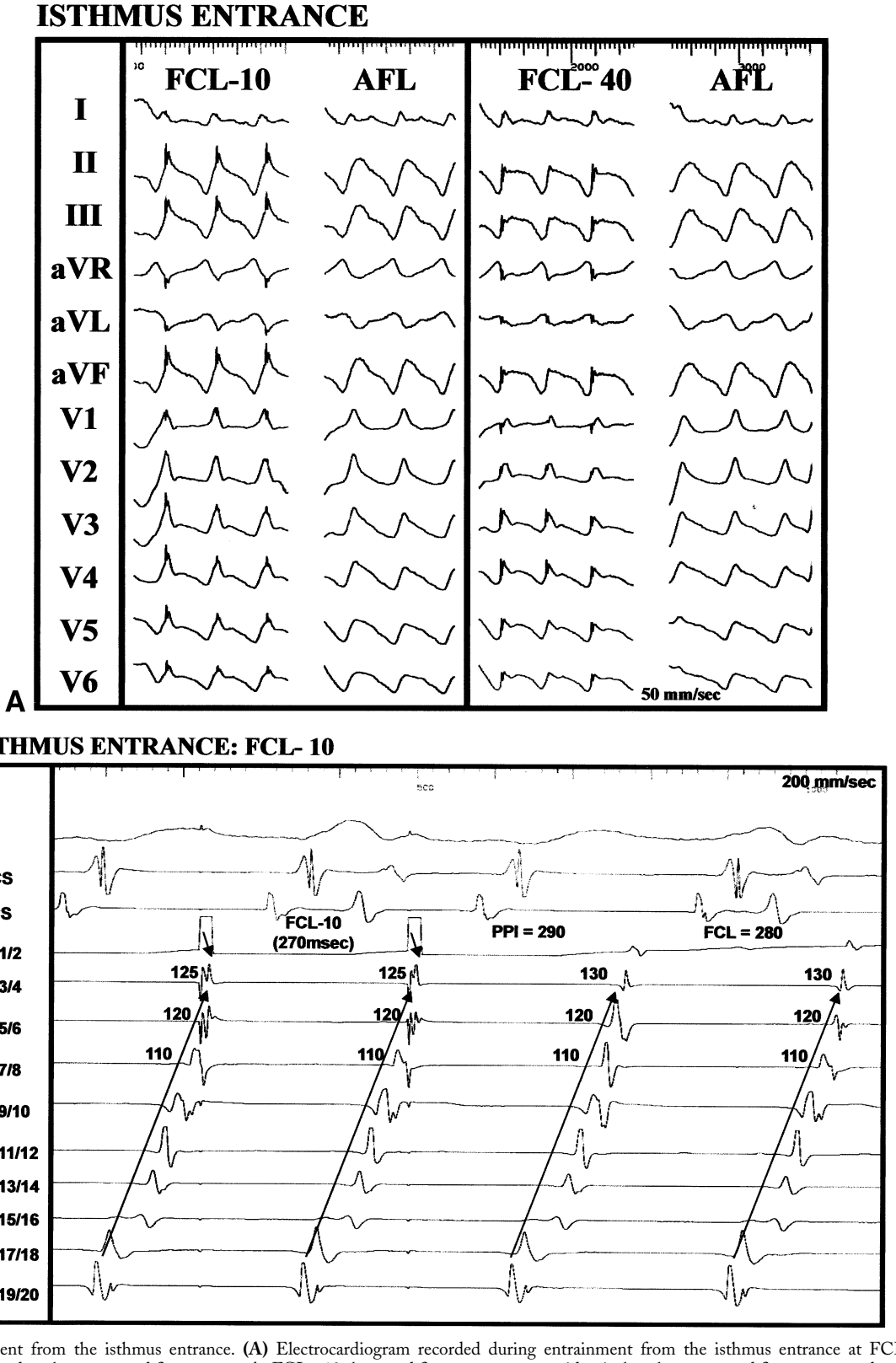

Figure 3. Entrainment from the isthmus entrance. **(A)** Electrocardiogram recorded during entrainment from the isthmus entrance at FCL−10 and FCL−40 ms compared to the non-paced flutter wave. At FCL−10 the paced flutter wave appears identical to the non-paced flutter wave and was recorded as concealed by three blinded observers. At FCL−40 the paced flutter wave is different from the non-paced flutter wave (note aVL and V1 in particular) and was recorded as manifest entrainment by three observers. **(B)** Intracardiac electrogram recording during entrainment at FCL−10 ms from the isthmus entrance (TA 1/2). Consistent capture could not be achieved from TA 5/6 on this occasion and the catheter was repositioned so that TA1/2 was now at the isthmus entrance. The PPI minus FCL is 10 ms confirming that this site is within the circuit. The upward arrows indicate the orthodromic activation times from TA 19/20 to TA 7/8 (110 ms), TA 5/6 (120 ms) and TA 3/4 (130 ms). During entrainment there is fusion between the antidromic **(downward arrows)** and orthodromic wavefronts at TA 3/4, which is now activated slightly earlier (125 ms).

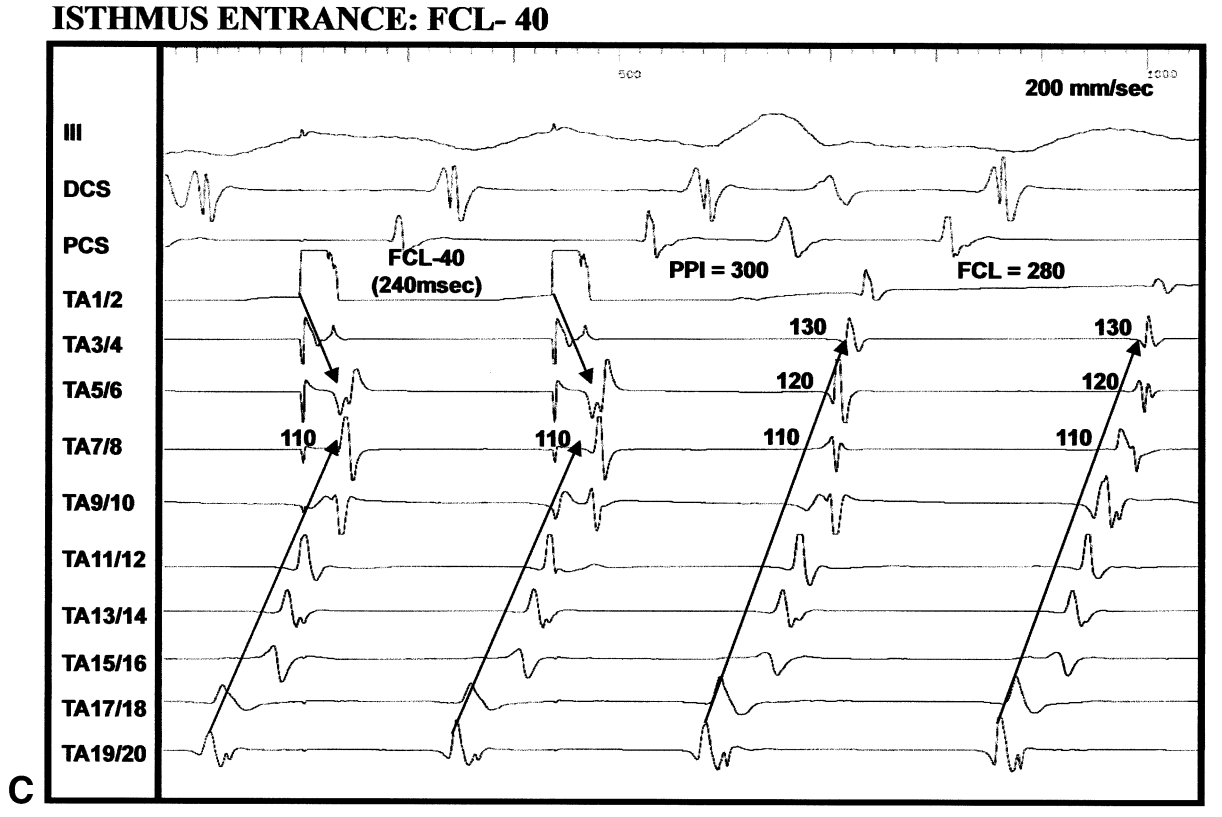

Figure 3. (*continued*) **(C)** Entrainment at FCL−40 ms from the isthmus entrance. The PPI minus FCL is 20 ms, confirming the site is within the circuit. TA 3/4 and 5/6 are now captured by the antidromic wave front **(downward arrows)** with associated electrogram morphology change and activation ahead of TA 7/8, which is still orthodromically activated (TA 19/20 to 7/8 activation time 110 ms), though with a slight electrogram morphology change suggesting possible fusion between the orthodromic and antidromic wave fronts at this site. Abbreviations as in Figure 2.

flutter terminated during entrainment pacing, and to 88% in the presence of split atrial electrograms or diastolic potentials. A limitation of using an unknown circuit such as an atypical right AFL to evaluate the utility of CE to identify an isthmus is that an RF application may be ineffective not only because it is incorrectly located but for other reasons including inadequate lesion size (either width or depth) or inadequate tissue heating. In addition, because RF applications will not be applied at sites demonstrating ME, the true specificity and negative predictive value cannot be calculated.

More recently a number of studies have compared the presence of CE with a circuit defined by an electroanatomic map in patients with "scar-mediated" atrial macro-reentry. Nakagawa et al. (22) performed entrainment mapping in six of 15 patients undergoing electroanatomic mapping of scar-mediated tachycardia. In these patients many sites within the circuit, but outside the isolated channel ("outer loop" site), exhibited entrainment with concealed fusion (same P-wave and activation sequence) and a PPI equal to the TCL. In 15 patients with repaired congenital heart disease and intra-atrial reentrant tachycardia undergoing electroanatomic mapping, Triedman et al. (23) found that the fraction of atrial endocardial points meeting entrainment criteria used in this study (PPI-TCL ≤20 ms at an entrainment rate of 5 to 25 ms below the tachycardia CL) was generally large, averaging 20% to 30%. Thus, the authors suggested that targeting sites for ablation solely by entrainment may have a low predictive value for success. In neither of these studies did the authors evaluate the effect of entrainment rate or systematically detail the sensitivity and specificity of CE for identification of a channel or isthmus.

By using a macro-reentrant tachycardia with a known circuit in the present study, a more accurate picture of the limitations of CE for the identification of an isthmus site could be obtained.

Is there an "ideal" entrainment rate? The present study demonstrates that whereas there may be no ideal entraining cycle length, there is instead an optimal CL that produces the best compromise. Furthermore, it may be best to utilize several entraining CL at a designated site in an attempt to improve diagnostic accuracy. Thus, pacing at a long CL (either FCL−10 or FCL−20) was associated with a 23% to 46% false-positive rate attributable to CE from non-isthmus circuit sites. The highest specificity (98%) was associated with pacing at shorter CLs (FCL = 40 ms), but at this rate isthmus entrance sites usually (70%) demonstrated ME. As such, at this CL certain isthmus sites may be inappropriately rejected as potential target sites for RFA. At an intermediate pacing rate of FCL−30, the sensitivity (85%) and specificity (90%) were more "balanced" than at other CLs,

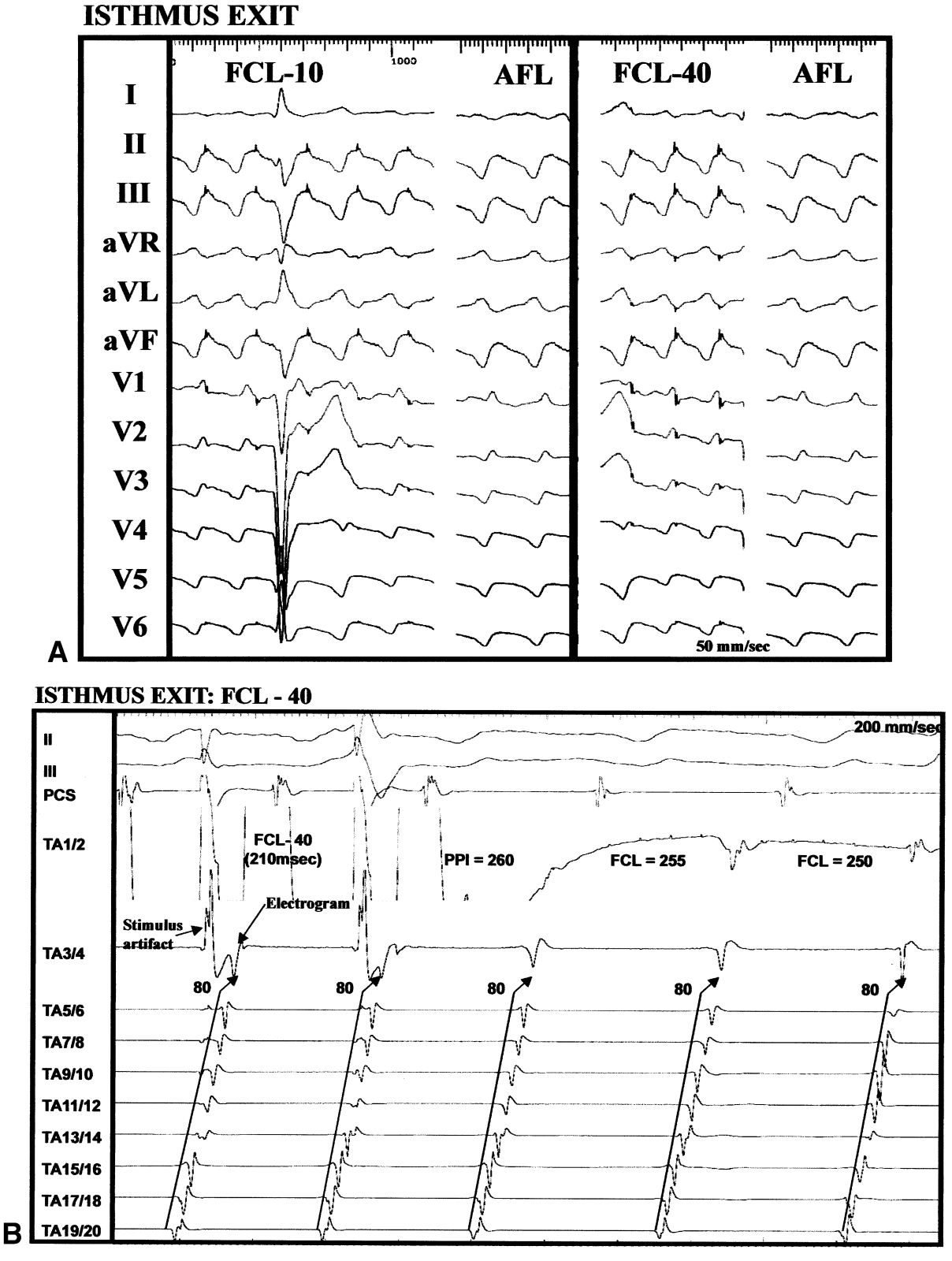

Figure 4. Entrainment from the isthmus exit. **(A)** Electrocardiogram recorded during entrainment from the isthmus exit at 10 ms and 40 ms below the flutter cycle length (FCL−10 and FCL−40) compared to the non-paced flutter wave. At both FCL−10 and FCL−40 the paced flutter wave appears identical to the non-paced flutter wave and was recorded as concealed by three blinded observers on both occasions. **(B)** Intracardiac electrogram recording during entrainment at FCL−40 ms from the isthmus exit (TA 1/2). The PPI minus FCL is 5 ms, confirming that this site is within the circuit. The upward arrows indicate the orthodromic activation time from TA 19/20 to TA 3/4 (80 ms), which is unchanged during entrainment consistent with orthodromic capture of TA 3/4. Allowing for the pacing spike artifact, there is no electrogram morphology change in TA 3/4 either.

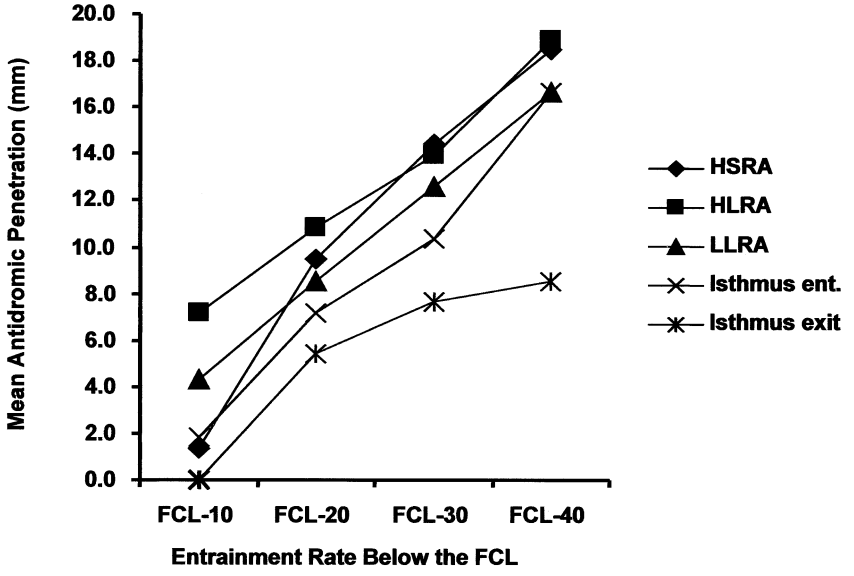

Figure 5. Mean antidromic penetration (AP) plotted against entrainment rate. When compared to other sites within the atrial flutter circuit, there was significant blunting ($p = 0.003$) in the extent of AP measured from the isthmus exit at entrainment rates of FCL−30 (8 ± 3 mm) and FCL−40 (9 ± 3 mm). FCL = flutter cycle length; HSRA/HLRA/LLRA = high septal, high lateral and low lateral right atrium.

but concealed fusion still resulted during entrainment from one of five non-isthmus sites in 50% of patients.

It has been demonstrated during entrainment of ventricular arrhythmias that entraining at faster rates may increase the PPI by decremental conduction within the circuit (6). In the current study, although there was a slight increase in the PPI when entraining at TCL-40 compared with TCL-10, this was not of sufficient magnitude to result in sites within the circuit falsely appearing "out."

Extent of antidromic penetration. The degree of AP significantly increased at all sites during pacing at progressively shorter CL and was significantly associated with the finding of fusion (ME) on the surface ECG ($p < 0.001$). The demonstration of increasing AP with increasing pacing rate represents fulfillment of the originally described fourth criteria for establishing the presence of transient entrainment, the electrogram equivalent of progressive fusion (4). The current study has quantified this variable (AP) in a known macro-reentrant circuit and systematically analyzed the relationship among AP, entrainment site, rate and presence/absence of surface ECG fusion.

Cosio et al. (17) have previously shown during entrainment of typical AFL from the high anterior RA that surface fusion may occur in the absence of significant AP if there is overlap of orthodromic septal activation by the n−1 wave front with anterior wall activation of the following cycle. This site-dependent effect would also be expected to be more prominent at shorter pacing CL (Fig. 2C).

In the present study, pacing from the isthmus exit produced almost 50% less AP than that measured from the isthmus entrance and other non-isthmus sites at the same rate. In typical AFL the isthmus, and in particular the medial isthmus, has been shown to be an area of slowed conduction, which would be expected to influence the extent of AP (10,15,17,24,25). In contrast, the absolute degree of AP from the lateral isthmus was not different at FCL−40 ms from the non-isthmus sites. Extrapolating these data to unknown atrial circuits implies that during entrainment at shorter CL from isthmus entrance sites, and possibly from some mid-isthmus sites, ME may result due to significant AP.

Limitations. In this study, the extent of AP was measured from a single multipolar catheter (TA catheter). If the AP occurred in a direction at an angle to this catheter, or if there was anisotropy of the extent of AP, this technique would provide an inaccurate assessment.

Conclusions. On the basis of this model, the diagnostic utility of CE for identification of an isthmus in the atrium is highly dependent on the pacing CL and the anatomic location of the site relative to the isthmus exit. Concealed entrainment is frequently observed at long CL from non-isthmus sites within the circuit, but may be absent from entrance isthmus sites at shorter CL. These findings may have implications for mapping of other macro-reentrant tachycardias where the location of the critical isthmus is unknown.

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REFERENCES

1. Waldo AL, Maclean WA, Karp RB, Kouchoukos NT, James TN. Entrainment and interruption of atrial flutter with atrial pacing: studies in man following open heart surgery. Circulation 1977;56:737–45.
2. Waldo AL, Henthorn RW, Plumb VJ, Maclean WA. Demonstration of the mechanism of transient entrainment and interruption of ventricular tachycardia with rapid atrial pacing. J Am Coll Cardiol 1984;3:422–30.
3. Waldo AL, Plumb VJ, Arciniegas JG, et al. Transient entrainment and interruption of the atrioventricular bypass pathway type of paroxysmal atrial tachycardia. A model for understanding and identifying reentrant arrhythmias. Circulation 1983;67:73–83.
4. Henthorn RW, Okumura K, Olshansky B, Plumb VJ, Hess PG, Waldo AL. A fourth criterion for transient entrainment: the electrogram equivalent of progressive fusion. Circulation 1988;77:1003–12.
5. Okumura K, Olshansky B, Henthorn RW, Epstein AE, Plumb VJ, Waldo AL. Demonstration of the presence of slow conduction during sustained ventricular tachycardia in man: use of transient entrainment of the tachycardia. Circulation 1987;75:369–78.
6. Stevenson WG, Khan H, Sager P, et al. Identification of reentry circuit sites during catheter mapping and radiofrequency ablation of ventricular tachycardia late after myocardial infarction. Circulation 1993;88:1647–70.
7. Kalman JM, VanHare GF, Olgin JE, Saxon LA, Stark SI, Lesh MD. Ablation of "incisional" reentrant atrial tachycardia complicating surgery for congenital heart disease. Use of entrainment to define a critical isthmus of conduction. Circulation 1996;93:502–12.
8. Kalman JM, Olgin JE, Saxon LA, Lee RJ, Scheinman MM, Lesh MD. Electrocardiographic and electrophysiologic characterization of atypical atrial flutter in man: use of activation and entrainment mapping and implications for catheter ablation. J Cardiovasc Electrophysiol 1997;8:121–44.
9. Lesh MD, VanHare G, Epstein LM, et al. Radiofrequency catheter ablation of atrial arrhythmias. Results and mechanisms. Circulation 1994;89:1074–89.
10. Feld GK, Fleck RP, Chen PS, et al. Radiofrequency catheter ablation for the treatment of human type 1 atrial flutter. Identification of a critical zone in the reentrant circuit by endocardial mapping techniques. Circulation 1992;86:1233–40.
11. Cosio FG, Lopez-Gil M, Goicolea A, Arribas F, Barroso JL. Radiofrequency ablation of the inferior vena cava-tricuspid valve isthmus in common atrial flutter. Am J Cardiol 1993;71:705–9.
12. El-Shalakany A, Hadjis T, Papageorgiou P, Monahan K, Epstein L, Josephson ME. Entrainment/mapping criteria for the prediction of termination of ventricular tachycardia by single radiofrequency lesion in patients with coronary artery disease. Circulation 1999;99:2283–9.
13. Morady F, Kadish A, Rosenheck S, et al. Concealed entrainment as a guide for catheter ablation of ventricular tachycardia in patients with prior myocardial infarction. J Am Coll Cardiol 1991;17:678–89.
14. Olgin JE, Kalman JM, Fitzpatrick AP, Lesh MD. Role of right atrial endocardial structures as barriers to conduction during human type I atrial flutter. Activation and entrainment mapping guided by intracardiac echocardiography. Circulation 1995;92:1839–48.
15. Shah DC, Jais P, Haissaguerre M, et al. Three-dimensional mapping of the common atrial flutter circuit in the right atrium. Circulation 1997;96:3904–12.
16. Nakagawa H, Lazzara R, Khastgir T, et al. Role of the tricuspid annulus and the eustachian valve/ridge on atrial flutter. Relevance to catheter ablation of the septal isthmus and a new technique for rapid identification of ablation success. Circulation 1996;94:407–24.
17. Cosio FG, Lopez GM, Arribas F, Palacios J, Goicolea A, Nunez A. Mechanisms of entrainment of human common flutter studied with multiple endocardial recordings. Circulation 1994;89:2117–25.
18. Waldo AL. Atrial flutter: entrainment characteristics. J Cardiovasc Electrophysiol 1997;8:337–52.
19. Simel DL, Samsa GP, Matchar DB. Likelihood ratios with confidence: sample size estimation for diagnostic test studies. J Clin Epidemiol 1991;44:763–70.
20. Rigby AS. Statistical methods in epidemiology. Towards an understanding of the kappa coefficient. Disability Rehabilitation 2000;22:339–44.
21. Bogun F, Bender B, Li YG, Hohnloser SH. Ablation of atypical atrial flutter guided by the use of concealed entrainment in patients without prior cardiac surgery. J Cardiovasc Electrophysiol 2000;11:136–45.
22. Nakagawa H, Shah N, Matsudaira K, et al. Characterization of reentrant circuit in macroreentrant right atrial tachycardia after surgical repair of congenital heart disease: isolated channels between scars allow "focal" ablation. Circulation 2001;103:699–709.
23. Triedman JK, Alexander ME, Berul CI, Bevilacqua LM, Walsh EP. Electroanatomic mapping of entrained and exit zones in patients with repaired congenital heart disease and intra-atrial reentrant tachycardia. Circulation 2001;103:2060–5.
24. Olshansky B, Okumura K, Hess PG, Waldo AL. Demonstration of an area of slow conduction in human atrial flutter. J Am Coll Cardiol 1990;16:1639–48.
25. Feld GK, Mollerus M, Birgersdotter-Green U, et al. Conduction velocity in the tricuspid valve-inferior vena cava isthmus is slower in patients with type I atrial flutter compared to those without a history of atrial flutter. J Cardiovasc Electrophysiol 1997;8:1338–48.